In the claims:

For the convenience of the Examiner, all claims being examined, whether or not amended, are presented below.

1. (Currently Amended) A method for modifying reducing the rate of, in an animal, metabolism of glucagon-like peptide 1 (GLP-1), comprising administering to the an animal a composition including one or more inhibitors of a dipeptidylpeptidase IV which inactivates GLP-1, wherein the inhibitor is represented by Formula I:

wherein

A represents a 4-8 membered heterocycle including the N and a $C\alpha$ carbon;

Z represents C or N;

W represents -CH=NR₅, a functional group which reacts with an active site residue of the targeted protease, or

R₁ represents a C-terminally linked amino acid residue or amino acid analog, or a C- terminally linked peptide or peptide analog, or an amino-protecting group, or

$$R_6$$
 R_6 R_6

R₂ is absent or represents one or more substitutions to the ring A, each of which can independently be a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a

thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, $-(CH_2)_m$ -R₇, $-(CH_2)_m$ -OH, $-(CH_2)_m$ -O-lower alkyl, $-(CH_2)_m$ -O-lower alkenyl, $-(CH_2)_m$ -O-(CH₂)_m-R₇, $-(CH_2)_m$ -SH, $-(CH_2)_m$ -S-lower alkyl, $-(CH_2)_m$ -S-lower alkenyl, or $-(CH_2)_n$ -S-(CH₂)_m-R₇;

- if Z is N, R₃ represents hydrogen, if Z is C, R₃ represents hydrogen or a halogen, a lower alkyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, -(CH₂)_m-R₇, (CH₂)_m-O-lower alkyl, -(CH₂)_m-O-lower alkenyl, -(CH₂)_m-O-(CH₂)_m-R₇, -(CH₂)_m-S-lower alkyl, -(CH₂)_m-S-lower alkenyl, or -(CH₂)_n-S-(CH₂)_m-R₇;
- R₅ represents a hydrogen, an alkyl, an alkenyl, an alkynyl, $-C(X_1)(X_2)X_3$, $-(CH_2)_m$ -R₇, $-(CH_2)_n$ -O-alkyl, $-(CH_2)_n$ -O-alkenyl, $-(CH_2)_n$ -O-alkynyl, $-(CH_2)_n$ -O-alkynyl, $-(CH_2)_n$ -S-alkyl, $-(CH_2)_n$ -S-alkenyl, $-(CH_2)_n$ -S-alkynyl, $-(CH_2)_n$ -S-alkynyl, $-(CH_2)_n$ -S-(CH₂)_m-R₇, $-C(O)C(O)NH_2$, or -C(O)C(O)OR'7;
- R_6 represents hydrogen, a halogen, an an alkyl, an an alkenyl, an an alkynyl, an aryl, -(CH₂)_m-R₇, -(CH₂)_m-O-alkyl, -(CH₂)_m-O-alkenyl, -(CH₂)_m-O-alkynyl, -(CH₂)_m-O-alkynyl, -(CH₂)_m-S-alkyl, -(CH₂)_m-S-alkyl, -(CH₂)_m-S-alkynyl, or -(CH₂)_m-S-(CH₂)_m-R₇,

R₇ represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl,

cycloalkenyl, or heterocycle;

R'7 represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

Rg and Rg each independently represent hydrogen, alkyl, alkenyl, - $(CH_2)_m$ -R7, -C(=O)-alkyl, -C(=O)-alkynyl, or -C(=O)- $(CH_2)_m$ -R7,

or R₈ and R₉ taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

R₅₀ represents O or S;

R₅₁ represents N₃, SH, NH₂, NO₂ or OR'₇;

R₅₂ represents hydrogen, a lower alkyl, an amine, OR'₇, or a pharmaceutically acceptable salt, or R₅₁ and R₅₂ taken together with the phosphorous atom to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

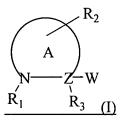
 $\underline{Y_1}$ and $\underline{Y_2}$ can independently or together be a group capable of being hydrolyzed to a hydroxyl group, or cyclic derivatives where $\underline{Y_1}$ and $\underline{Y_2}$ are connected via a ring having from 5 to 8 atoms in the ring structure;

X₁ represents a halogen;

X₂ and X₃ each represent a hydrogen or a halogen;

m is zero or an integer in the range of 1 to 8; and n is an integer in the range of 1 to 8.

2. (Currently Amended) A method for modifying improving glucose metabolism of an animal tolerance, comprising administering to the an animal a composition including one or more protease inhibitors which inhibit DPIV-mediated proteolysis dipeptidylpeptidase IV, wherein the inhibitor is represented by Formula I:



wherein

A represents a 4-8 membered heterocycle including the N and a Cα carbon;

Z represents C or N;

W represents -CH=NR5,

R₁ represents a C-terminally linked amino acid residue or amino acid analog, or a C- terminally linked peptide or peptide analog, or an amino-protecting group, or

$$R_6$$
 S_5 , R_6 S_5 , or R_6 S_5

R₂ is absent or represents one or more substitutions to the ring A, each of which can independently be a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, -(CH₂)_m-R₇, -(CH₂)_m-OH, -(CH₂)_m-O-lower alkyl, - (CH₂)_m-O-lower alkenyl, -(CH₂)_n-O-(CH₂)_m-R₇, -(CH₂)_m-SH, -(CH₂)_m-S-lower alkyl, -(CH₂)_m-S-lower alkenyl, or -(CH₂)_n-S-(CH₂)_m-R₇;

- if Z is N, R₃ represents hydrogen, if Z is C, R₃ represents hydrogen or a halogen, a lower alkyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, -(CH₂)_m-R₇, (CH₂)_m-O-lower alkyl, -(CH₂)_m-O-lower alkenyl, -(CH₂)_m-O-(CH₂)_m-R₇, -(CH₂)_m-S-lower alkyl, -(CH₂)_m-S-lower alkenyl, or -(CH₂)_n-S-(CH₂)_m-S-(CH₂)
- R₅ represents a hydrogen, an alkyl, an alkenyl, an alkynyl, $-C(X_1)(X_2)X_3$, $-(CH_2)_m-R_7$, $-(CH_2)_n-O-alkyl$, $-(CH_2)_n-O-alkyl$, $-(CH_2)_n-O-alkyl$, $-(CH_2)_n-O-alkyl$, $-(CH_2)_n-O-alkyl$, $-(CH_2)_n-S-alkyl$, $-(CH_2)_n-S-al$
- $R_{\underline{6}}$ represents hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, -(CH₂)_m-R₇, (CH₂)_m-O-alkyl, -(CH₂)_m-O-alkynyl, -(CH₂)_m

 $\frac{(CH_2)_m-R_7, -(CH_2)_m-SH, -(CH_2)_m-S-alkyl, -(CH_2)_m-S-alkenyl, -(CH_2)_m-S-alkynyl,}{\text{or } -(CH_2)_m-S-(CH_2)_m-R_7}$

- <u>R7</u> represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkyl, cycloalkenyl, or heterocycle;
- R'7 represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;
- Rg and Rg each independently represent hydrogen, alkyl, alkenyl, -(CH2) \underline{m} -R7, -C(=O)-alkyl, -C(=O)-alkynyl, or -C(=O)-(CH2) \underline{m} -R7.
- or R₈ and R₉ taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

R₅₀ represents O or S;

R51 represents N3, SH, NH2, NO2 or OR'7;

- R₅₂ represents hydrogen, a lower alkyl, an amine, OR'₇, or a pharmaceutically acceptable salt, or R₅₁ and R₅₂ taken together with the phosphorous atom to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;
- Y₁ and Y₂ can independently or together be a group capable of being hydrolyzed to a hydroxyl group, or cyclic derivatives where Y₁ and Y₂ are connected via a ring having from 5 to 8 atoms in the ring structure;

X₁ represents a halogen;

X2 and X3 each represent a hydrogen or a halogen;

m is zero or an integer in the range of 1 to 8; and n is an integer in the range of 1 to 8.

3. (Currently Amended) A-The method of claim 2, wherein said for modifying glucose metabolism of an animal, comprising administering to the animal a composition including one or more protease inhibitors which inhibit the proteolysis of glucagon like peptide 1 (GLP-1) and

accordingly-increase the plasma half-life of GLP-1in the animal. wherein the inhibitor is represented by Formula I

4. (Currently Amended) A method for treating Type II diabetes, comprising administering to an animal a composition including one or more inhibitors of dipeptidylpeptidase IV (DPIV) represented by Formula I:

wherein

A represents a 4-8 membered heterocycle including the N and a Cα carbon;

Z represents C or N;

W represents -CH=NR₅,

R₁ represents a C-terminally linked amino acid residue or amino acid analog, or a C- terminally linked peptide or peptide analog, or an amino-protecting group, or

$$R_6$$
 S^{S} , R_6 S^{S} , or R_6 S^{S}

R2 is absent or represents one or more substitutions to the ring A, each of which can

independently be a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, -(CH₂)_m-R₇, -(CH₂)_m-OH, -(CH₂)_m-O-lower alkyl, - (CH₂)_m-O-lower alkenyl, -(CH₂)_m-C-(CH₂)_m-R₇, -(CH₂)_m-SH, -(CH₂)_m-S-lower alkyl, -(CH₂)_m-S-lower alkenyl, or -(CH₂)_n-S-(CH₂)_m-R₇;

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- if Z is N, R₃ represents hydrogen, if Z is C, R₃ represents hydrogen or a halogen, a lower alkyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, -(CH₂)_m-R₇, (CH₂)_m-O-lower alkyl, -(CH₂)_m-O-lower alkenyl, -(CH₂)_m-O-(CH₂)_m-R₇, -(CH₂)_m-S-lower alkyl, -(CH₂)_m-S-lower alkenyl, or -(CH₂)_n-S-(CH₂)_m-S-(CH₂)
- R5 represents a hydrogen, an alkyl, an alkenyl, an alkynyl, -C(X_1)(X_2) X_3 , -(CH₂)_m-R₇, (CH₂)_n-O-alkyl, -(CH₂)_n-O-alkynyl, -(CH₂)_n-O-alkynyl, -(CH₂)_n-O-alkynyl, -(CH₂)_n-S-alkyl, -(CH₂)_n-S-alkynyl, -(CH₂)_n-S-alkynyl, -(CH₂)_n-S-alkynyl, -(CH₂)_n-S-(CH₂)_m-R₇, -C(O)C(O)NH₂, or -C(O)C(O)OR'₇;
- $\begin{array}{c} \underline{R_6} \text{ represents hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, -(CH$_2$)$_{\underline{m}}-R$_{\underline{7}}, -\\ & \underline{(CH$_2$)$_{\underline{m}}-OH, -(CH$_2$)$_{\underline{m}}-O-alkyl, -(CH$_2$)$_{\underline{m}}-O-alkynyl, -(CH$_2$)$_{\underline{m}}-O-alkynyl, -(CH$_2$)$_{\underline{m}}-S-alkynyl, -(CH$_2$)$_{\underline{m}}-S-alkynyl, -(CH$_2$)$_{\underline{m}}-S-alkynyl, -(CH$_2$)$_{\underline{m}}-S-alkynyl, -(CH$_2$)$_{\underline{m}}-S-(CH$_2$)$_{\underline{m}}-S-(CH$_2$)$_{\underline{m}}-R$_{\underline{7}}. \end{array}$

- <u>R7</u> represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl, or heterocycle;
- R'7 represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;
- <u>R8</u> and <u>R9</u> each independently represent hydrogen, alkyl, alkenyl, -(CH2) \underline{m} -R7, -C(=O)-alkyl, -C(=O)-alkynyl, or -C(=O)-(CH2) \underline{m} -R7.
- or R₈ and R₉ taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

R₅₀ represents O or S;

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R51 represents N3, SH, NH2, NO2 or OR'7;

R₅₂ represents hydrogen, a lower alkyl, an amine, OR'₇, or a pharmaceutically acceptable salt, or R₅₁ and R₅₂ taken together with the phosphorous atom to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

Y₁ and Y₂ can independently or together be a group capable of being hydrolyzed to a hydroxyl group, or cyclic derivatives where Y₁ and Y₂ are connected via a ring having from 5 to 8 atoms in the ring structure;

X₁ represents a halogen;

X₂ and X₃ each represent a hydrogen or a halogen; m is zero or an integer in the range of 1 to 8; and n is an integer in the range of 1 to 8.

- 5. (Currently Amended) The method of claim 1 or 2, wherein the dipeptidylpeptidase is DPIV animal is a mammal.
- 6. (Currently Amended) The method of claim 35, wherein the protease inhibitor is an inhibitor of DPIV mammal is a human.
- 7. (Previously Amended) The method of claim 2 or 3, wherein administering the inhibitor reduces one or more of insulin resistance, glucose intolerance, hyperglycemia, hyperinsulinemia, obesity, hyperlipidemia, or hyperlipoproteinemia.
- 8. (Previously Amended) The method of claim 1, 2, 3 or 4, wherein the inhibitor has an EC_{50} for modification of glucose metabolism which is at least one order of magnitude less than its EC_{50} for immunosuppression.
- 9. (Currently Amended) The method of claim 1, 2, 3 or 4, wherein the inhibitor has an EC₅₀ for inhibition of glucose intolerance in the nanomolar or less range.
- 10. (Currently Amended) The method of claim 8, wherein the inhibitor has an EC₅₀ for immunosuppression in the μM micromolar or greater range.

- 11. (Previously Amended) The method of claim 4, 5-or 6, wherein the inhibitor has a Ki for DPIV inhibition of 1.0 nM or less.
- 12. (Previously Amended) The method of claim 1, 2, 3 or 4, wherein the inhibitor is peptidomimetic of a peptide selected from Pro-Pro, Ala-Pro, and (D)-Ala-(L)-Ala.
- 13. (Previously Amended) The method of claim 1, 2, 3 or 4, wherein the inhibitor has a molecular weight less than 7500 amu.
- 14. (Previously Amended) The method of claim 1, 2, 3 or 4, wherein the inhibitor is administered orally.
- 15. (Cancelled)
- 16. (Currently Amended) The method of claim 1, 2, 3, or 4, wherein W represents -CH=NR₅,

- R₅ represents H, an alkyl, an alkenyl, an alkynyl, $-C(X_1)(X_2)X_3$, $-(CH_2)m-R_7$, $-(CH_2)n-OH$, $-(CH_2)n-O-alkyl$, $-(CH_2)n-O-alkyl$, $-(CH_2)n-O-alkynyl$, $-(CH_2)n-O-(CH_2)m-R_7$, $-(CH_2)n-SH$, $-(CH_2)n-S-alkyl$, $-(CH_2)n-S-alkynyl$, $-(CH_2)n-S-alkynyl$, $-(CH_2)n-S-alkynyl$, $-(CH_2)m-R_7$, $-C(O)C(O)NH_2$, or $-C(O)C(O)OR^3$;
- R7 represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;
- R'7 represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl, or heterocycle;

Y₁ and Y₂ can independently or together be OH, or a group capable of being hydrolyzed to a hydroxyl group, including or cyclic derivatives where Y₁ and Y₂ are connected via a ring having from 5 to 8 atoms in the ring structure;

R₅₀ represents O or S;

R₅₁ represents N₃, SH, NH₂, NO₂ or OR'₇;

R₅₂ represents hydrogen, a lower alkyl, an amine, OR'₇, or a pharmaceutically acceptable salt, or R₅₁ and R₅₂ taken together with the phosphorous atom to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

X₁ represents a halogen;

X₂ and X₃ each represent a hydrogen or a halogen; m is zero or an integer in the range of 1 to 8; and n is an integer in the range of 1 to 8.

17. (Previously Amended) The method of claim 16, wherein the ring A is represented by the formula:

$$-N$$

wherein n is an integer of 1 or 2.

18. (Previously Amended) The method of claim 16, wherein W

$$-B \begin{pmatrix} Y_1 \\ Y_2 \end{pmatrix} \text{ or } R5$$
 represents

19. (Original) The method of claim 16, wherein R₁ represents

 R_{36} is a small hydrophobic group and R_{38} is hydrogen, or, R_{36} and R_{38} together form a 4-7 membered heterocycle including the N and the $C\alpha$ carbon, as defined for A above; and

R₄₀ represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino-protecting group.

- 20. (Previously Amended) The method of claim 16, wherein R_2 is absent, or represents a small hydrophobic group.
- 21. (Previously Amended) The method of claim 16, wherein R₃ is a hydrogen, or a small hydrophobic group.
- 22. (Previously Amended) The method of claim 16, wherein R_5 is a hydrogen, or a halogenated lower alkyl.
- 23. (Previously Amended) The method of claim 16, wherein X_1 is a fluorine, and X_2 and X_3 , if halogens, are fluorine.
- 24. (Currently Amended) The method of claim 16, wherein the inhibitor is represented by the general formula:

$$R1$$
 OR_{12}
 OR_{13}

wherein

R₁ represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino protecting group, or

 R_6 represents hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, -(CH2)_m-R7, - $(CH_2)_m\text{-O-alkyl}, \text{-(CH}_2)_m\text{-O-alkynyl}, \text{-(CH}_2)_m\text{-O-alkynyl}, \text{-(CH}_2)_m\text{-O-alkynyl}, \text{-(CH}_2)_m\text{-S-alkynyl}, \text{-(CH}_2)_m\text{-S-alkynyl}, \text{-(CH}_2)_m\text{-S-alkynyl}, \text{-(CH}_2)_m\text{-S-(CH}_2)_m\text{-R7},$

R7 represents an aryl, a cycloalkyl, a cycloalkenyl, or a heterocycle;

R₈ and R₉ each independently represent hydrogen, alkyl, alkenyl, -(CH₂)_m-R₇, -C(=O)-alkyl, -C(=O)-alkynyl, or -C(=O)-(CH₂)_m-R₇,

or R₈ and R₉ taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

R₁₁ and R₁₂ each independently represent hydrogen, an alkyl, or a pharmaceutically acceptable salt, or R₁₁ and R₁₂ taken together with the O-B-O atoms to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure; m is zero or an integer in the range of 1 to 8; and n is an integer in the range of 1 to 8.

25. (Currently Amended) The method of claim 16, wherein the inhibitor is represented by the general formula

wherein

R₁ represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino protecting group, or

 R_6 represents hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, $-(CH_2)_m$ - R_7 , $-(CH_2)_m$ -O-alkyl, $-(CH_2)_m$ -O-alkynyl, $-(CH_2)_m$ -O-alkynyl, $-(CH_2)_m$ -O-alkynyl, $-(CH_2)_m$ -S-alkynyl, $-(CH_2)_m$ -S-alkynyl, $-(CH_2)_m$ -S-alkynyl, $-(CH_2)_m$ -S-alkynyl, $-(CH_2)_m$ -S-($-(CH_2)_m$ -S-alkynyl, $-(CH_2)_m$ -S-alkynyl, $-(CH_2)_m$ -S-($-(CH_2)_m$ -S-alkynyl), $-(CH_2)_m$ -S-($-(CH_2)_m$ -S-alkynyl), $-(CH_2)_m$ -S-alkynyl, $-(CH_2)_m$ -S-

$$-(CH_{2})_{m}-N { \begin{array}{c} R_{8} \\ R_{9} \end{array}}, \quad -(CH_{2})_{n}-C-N { \begin{array}{c} R_{8} \\ R_{9} \end{array}}, \quad -(CH_{2})_{n}-NH_{2}-C-NH_{2} \end{array}, \quad -(CH_{2})_{n}-C-O-R_{7}$$

R7 represents an aryl, a cycloalkyl, a cycloalkenyl, or a heterocycle;

R₈ and R₉ each independently represent hydrogen, alkyl, alkenyl, -(CH₂)_m-R₇, -C(=O)-alkyl, -C(=O)-alkynyl, or -C(=O)-(CH₂)_m-R₇,

or R₈ and R₉ taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure; m is zero or an integer in the range of 1 to 8; and n is an integer in the range of 1 to 8.

26. (Currently Amended) The method of claim 16, wherein the inhibitor is represented by the general formula:

$$\begin{array}{c} & & & \\ & & \\ & & & \\ & & & \\ & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & &$$

wherein

R₁ represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino protecting group, or

$$R_6$$
 S^{c} , R_6 S^{c} , or R_6 S^{c} S^{c} ;

 R_6 represents hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, $-(CH_2)_m$ - R_7 , $-(CH_2)_m$ - $-(CH_2$

$$-(CH_2)_m-N {\begin{matrix} R_8 \\ R_9 \end{matrix}}, \quad -(CH_2)_n-C-N {\begin{matrix} R_8 \\ R_9 \end{matrix}}, \quad -(CH_2)_n-NH_2-C-NH_2 \ , \quad -(CH_2)_n-C-O-R_7$$

R7 represents an aryl, a cycloalkyl, a cycloalkenyl, or a heterocycle;

Rg and R9 each independently represent hydrogen, alkyl, alkenyl, - $(CH_2)_m$ -R7, -C(=O)-alkyl, -C(=O)-alkynyl, or -C(=O)-($CH_2)_m$ -R7,

or R₈ and R₉ taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

X₁, X₂ and X₃ each represent a hydrogen or a halogen;

m is zero or an integer in the range of 1 to 8; and n is an integer in the range of 1 to 8.

27. (Currently Amended) The method of claim 16, wherein the inhibitor is represented by the general formula:

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wherein

A represent a 4-8 membered heterocycle including an N and a $C\alpha$ carbon;

W represents, -CH=NR5;

R₂ is absent or represents one or more substitutions to the ring A, each of which can independently be a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, -(CH₂)_m-R₇, -(CH₂)_m-OH, -(CH₂)_m-O-lower alkyl, -(CH₂)_m-O-lower alkenyl, -(CH₂)_n-O-(CH₂)_m-R₇, -(CH₂)_m-SH, -(CH₂)_m-S-lower alkyl, -(CH₂)_m-S-lower alkenyl, or -(CH₂)_n-S-(CH₂)_m-R₇:

R₃ represents a hydrogen or a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, -(CH₂)_m-R₇, -(CH₂)_m-OH, -(CH₂)_m-O-lower alkyl, -(CH₂)_m-O-lower alkenyl, -(CH₂)_m-O-(CH₂)_m-R₇, -(CH₂)_m-SH, -(CH₂)_m-S-lower alkyl, -(CH₂)_m-S-lower alkenyl, or -(CH₂)_n-S-(CH₂)_m-R₇;

R₅ represents a hydrogen, an alkyl, an alkenyl, an alkynyl, $-C(X_1)(X_2)X_3$, $-(CH_2)_m-R_7$, $-(CH_2)_n-O-alkyl$, $-(CH_2)_n-O-alkyl$, $-(CH_2)_n-O-alkynyl$, $-(CH_2)_n-O-alkynyl$, $-(CH_2)_n-S-alkyl$, $-(CH_2)_n-S-alkynyl$

R7 represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

R'7 represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

R₃₂ is a small hydrophobic group;

R₃₀ represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino-protecting group- or

$$R_6$$
 S^{s} , R_6 S^{s} , or R_6 S^{s}

R₅₀ represents O or S;

R₅₁ represents N₃, SH, NH₂, NO₂ or OR'₇;

R₅₂ represents hydrogen, a lower alkyl, an amine, OR'7, or a pharmaceutically acceptable salt, or R₅₁ and R₅₂ taken together with the phosphorous atom to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

X₁ represents a halogen;

X₂ and X₃ each represent a hydrogen or a halogen;

m is zero or an integer in the range of 1 to 8; and

n is an integer in the range of 1 to 8.

28. (Currently Amended) A method for modifying, in an animal, metabolism of glucagonlike peptide 1 (GLP-1), comprising administering to the animal a composition including one or more inhibitors of a dipeptidylpeptidase which inactivates GLP-1,, wherein the inhibitor is represented by Formula II:

$$\begin{array}{c|c}
R_{1} & H & L & W \\
\hline
R_{1} & R_{61} & H & L & W \\
\hline
R_{1} & R_{61} & H & L & W \\
\hline
R_{1} & R_{62} & O & R_{62} & (II)
\end{array}$$

wherein

W represents a functional group which reacts with an active site residue of the targeted protease, selected from -CN, -CH=NR₅,

R₁ represents a C-terminally linked amino acid residue or amino acid analog, or a C- terminally linked peptide or peptide analog, or an amino-protecting group, or

$$R_6-C-, R_6-C-, R_6-S-$$

R₃ represents hydrogen or a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, -(CH₂)_m-R₇, -(CH₂)_m-OH, -(CH₂)_m-O-lower alkyl, - (CH₂)_m-O-lower alkenyl, -(CH₂)_m-O-(CH₂)_m-R₇, -(CH₂)_m-SH, -(CH₂)_m-S-lower alkyl, -(CH₂)_m-S-lower alkenyl, or -(CH₂)_n-S-(CH₂)_m-R₇;

R5 represents H, an alkyl, an alkenyl, an alkynyl, $-C(X_1)(X_2)X_3$, $-(CH_2)m-R_7$, $-(CH_2)n-OH$, $-(CH_2)n-O-alkyl$, $-(CH_2)n-O-alkynyl$, $-(CH_2)n-O-(CH_2)m-R_7$, $-(CH_2)n-SH$, $-(CH_2)n-S-alkyl$, $-(CH_2)n-S-alkynyl$, $-(CH_2)n-S-alk$

 R_6 represents hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, - $(CH_2)_m$ - R_7 , - $(CH_2)_m$

 $(CH_2)_m$ -R₇, - $(CH_2)_m$ -SH, - $(CH_2)_m$ -S-alkyl, - $(CH_2)_m$ -S-alkenyl, - $(CH_2)_m$ -S-alkynyl, or - $(CH_2)_m$ -S- $(CH_2)_m$ -R₇;

R7 represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl, or heterocycle;

R'7 represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl, or heterocycle;

R₆₁ and R₆₂, independently, represent small hydrophobic groups;

Y₁ and Y₂ can independently or together be OH, or a group capable of being hydrolyzed to a hydroxyl group, including or cyclic derivatives where Y₁ and Y₂ are connected via a ring having from 5 to 8 atoms in the ring structure;

R₅₀ represents O or S;

R₅₁ represents N₃, SH, NH₂, NO₂ or OR'₇;

R₅₂ represents hydrogen, a lower alkyl, an amine, OR'₇, or a pharmaceutically acceptable salt, or R₅₁ and R₅₂ taken together with the phosphorous atom to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

X₁ represents a halogen;

X₂ and X₃ each represent a hydrogen or a halogen;

m is zero or an integer in the range of 1 to 8; and n is an integer in the range of 1 to 8.

29. (Currently Amended) A method for modifiyingmodifying, in an animal, metabolism of peptide hormone, comprising administering to the animal a composition including one or more boronyl peptidomimetic inhibitors of dipeptidylpeptidase IV (DPIV) in an amount sufficient to increase the plasma half-life of a peptide hormone, which peptide hormone is selected from the group consisting of glucagon-like peptide 2 (GLP-2), growth hormone-releasing factor (GHRF), vasoactive intestinal peptide (VIP), peptide histidine isoleucine (PHI), pituitary adenylate cyclase activating peptide (PACAP), gastric inhibitory peptide (GIP), helodermin, Peptide YY and neuropeptide Y.

- 30. (Currently Amended) A method for modifying glucose metabolism of an animal, comprising administering to the animal a composition including <u>a</u> boronyl peptidomimetic of a peptide selected from Pro-Pro, Ala-Pro, and (D)-Ala-(L)-Ala.
- 31. (Currently Amended) The method of claim 3130, wherein the boronyl peptidomimetic is represented in the general formula:

wherein

each A independently represents a 4-8 membered heterocycle including the N and a $C\alpha$ carbon; R_2 is absent or represents one or more substitutions to the ring A, each of which can

independently be a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, -(CH₂)_m-R₇, -(CH₂)_m-OH, -(CH₂)_m-O-lower alkyl, - (CH₂)_m-O-lower alkenyl, -(CH₂)_n-O-(CH₂)_m-R₇, -(CH₂)_m-SH, -(CH₂)_m-S-lower alkyl, -(CH₂)_m-S-lower alkenyl, or -(CH₂)_n-S-(CH₂)_m-R₇;

R₃ represents hydrogen or a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, $-(CH_2)_m-O-lower$ alkyl, $-(CH_2)_m-O-lower$ alkenyl, $-(CH_2)_m-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S-lower$ alkyl, $-(CH_2)_m-S-lower$ alkenyl, or $-(CH_2)_n-S-(CH_2)_m-R_7$;

- R₅ represents H, an alkyl, an alkenyl, an alkynyl, -C(X₁)(X₂)X₃, -(CH₂)m-R₇, -(CH₂)n-OH, -(CH₂)n-O-alkyl, -(CH₂)n-O-alkynyl, -(CH₂)n-O-(CH₂)m-R₇, -(CH₂)n-S-alkyl, -(CH₂)n-S-alkynyl, -(CH₂)n
- R_6 represents hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, -(CH₂)_m-R₇, (CH₂)_m-O+alkyl, -(CH₂)_m-O-alkenyl, -(CH₂)_m-O-alkynyl, -(CH₂)_m-O-alkynyl, -(CH₂)_m-S-alkyl, -(CH₂)_m-S-alkynyl, or -(CH₂)_m-S-(CH₂)_m-R₇;
- R7 represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl, or heterocycle;
- R₃₀ represents a C-terminally linked amino acid residue or amino acid analog, or a C- terminally linked peptide or peptide analog, or an amino-protecting group, or

$$R_6 - C - , R_6 - C - , R_6 - C - , R_6 - C - ;$$

 R_{32} and $R_{61}R_{62}$, independently, represent small hydrophobic groups;

 Y_1 and Y_2 can independently or together be OH, or a group capable of being hydrolyzed to a hydroxyl group, includingor cyclic derivatives where Y_1 and Y_2 are connected via a ring having from 5 to 8 atoms in the ring structure;

m is zero or an integer in the range of 1 to 8; and n is an integer in the range of 1 to 8.

- 32. (Currently Amended) The method of claim 31, wherein administering the boronyl peptidomimetic reduces one or more of insulin resistance, glucose intolerance, hyperglycemia, hyperinsulinemia, obesity, hyperlipidemia, or hyperlipoproteinemia.
- 33. (Previously Amended) The method of claim 31, wherein the boronyl peptidomimetic has an EC_{50} for modification of glucose metabolism which is at least one order of magnitude less than its EC_{50} for immunosuppression.

- 34. (Previously Amended) The method of claim 31, wherein the boronyl peptidomimetic has an EC_{50} for inhibition of glucose tolerance in the nanomolar or less range.
- 35. (Previously Amended) The method of claim 31, wherein the boronyl peptidomimetic has an EC₅₀ for immunosuppression in the μ M or greater range.
- 36. (Previously Amended) The method of claim 31, wherein the boronyl peptidomimetic is administered orally.
- 37. (Currently Amended) A method for modifying glucose metabolism of an animal, comprising administering to the animal a composition comprising a peptidomimetic boronyl inhibitor wherein the peptide to be mimicked is Pro-Pro, Ala-Pro, and or (D)-Ala-(L)-Ala.
- 38. (New) The method of claim 6, wherein the human is a Type II diabetic.